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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,749	07/21/2006	Dan Peters	2815-0376PUS1	7821

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EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1624	

NOTIFICATION DATE	DELIVERY MODE
09/08/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/586,749	PETERS ET AL.	
	Examiner	Art Unit	
	NOBLE JARRELL	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *12-15,17-22 and 27-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,16,23-26 and 34-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :21 Jul 2006; 14 May 2008; 12 February 2009.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group II in the reply filed on 4 May 2009 is acknowledged.

Claim Objections

2. Claims 1-11, 16, 23-26, and 34-43 are objected to because of the following informalities: these claims have been searched only with respect to the elected group. Compounds of formula (I) have only been searched this much because compounds encompassed by groups I-IX of the 2 April 2009 restriction each require separate structural queries. Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-11, 16, 23-26, and 34-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for amides and esters of formula (I), does not reasonably provide enablement for all prodrugs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to compounds composed of a diazabicyclic ring connected to a .C(O)-furan-phenylene-NH(CO)-(phenyl or cyclopropyl) moiety and pharmaceutical compositions comprising the same.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Jantzen and Robinson (*Modern Pharmaceutics*, **1996**, page 596) that prodrug development requires undue experimentation because each new prodrug is considered a new entity and requires safety testing.

(5) The relative skill of those in the art:

Those of relative skill in the art are those with level of skill of the authors of the references cited to support the examiner's position. The relative skill of those in this art is MD's, PhD's, or those with advanced degrees and the requisite experience in preparation of prodrugs of formula (I).

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for preparation of amides and esters of formula (I).

However, the specification does not provide guidance for preparation of all prodrugs encompassed by formula (I).

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 1-11, 16, 23-26, and 34-43, and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

5. Claims 35-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the *in vitro* inhibition of ^{3}H-α-Bungarotoxine binding, does not reasonably provide enablement for the *in vivo* treatment, prevention, or alleviation of a disease or disorder responsive to modulation of a cholinergic receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to treatment, prevention, or alleviation of a cholinergic receptor modulated disorder with a compound composed of a diazabicyclic ring connected to a .C(O)-furan-phenylene-NH(CO)-(phenyl or cyclopropyl) moiety. Thus, the claims taken together with the specification imply a compound of the elected group can treat a cholinergic receptor modulated disease *in vivo*.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Livingstone et al. (*Biochemical Pharmacology*, **2009**, *78*, 744-55) teach that future research is needed to understand nicotinic acetylcholine receptors (page 751, section 6). Nicotinic acetylcholine receptors are one type of cholinergic receptors. As one example of a disorder which is not fully understand, Livingstone et al. cite addiction (page 751, section 6).

Alzheimer's disease (one example of a central nervous system condition) cannot be prevented (Pulley et al. US 7067507, column 2, lines 40-44).

(5) The relative skill of those in the art:

Those of relative skill in the art are those with level of skill of the authors of the references cited to support the examiner's position. The relative skill of those in this art is MD's, PhD's, or those with advanced degrees and the requisite experience in treatment, prevention, or alleviation of a disease or disorder which is responsive to modulation of a cholinergic receptor.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for the *in vitro* inhibition of ^{3}H-α-Bungarotoxine binding (page 32 of the specification).

However, the specification does not provide guidance for the *in vivo* treatment, prevention, or alleviation of a disease or disorder responsive to modulation of a cholinergic receptor.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 35-43 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 35-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 35 does not specify what type of disorder applicants intend to treat with a compound of claim 1. The only limitation is that a cholinergic receptor is being modulated. Claim 36 is unclear with respect to what disease applicants intend to treat. Do applicants mean Alzheimer's disease, Parkinson's disease, or trauma, for example? In claim 38, the method is associated with another disorder. This type of claim can be interpreted as treatment of a disorder that could be indirectly or directly associated with another disorder. The same issue applies to claims 39 and 43. Thus, the disease applicants are trying to treat could be secondary.

8. Regarding claims 37, 39, 40, 41 and 43, the phrases "such as" and "including" render the claims indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). The term "including" is interpreted the same as "such as" because it is not a closed term.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1-11, 16, 23-26, and 34-43 rejected under 35 U.S.C. 102(e) as being anticipated by Peters et al. (WO 2004/076453, published 10 September 2004, international filing date of 4 February 2004, has priority to 60/449871, filed 27 February 2003). Peters et al. teach compound 23 (of page 11). In this compound instant variable n is two, A' is furan, L is a bond, A" is phenylene, and B is NH(CO)phenyl. Pharmaceutical compositions are taught from pages 19 to 20. Compound 23 is prepared on page 21 (example 1). This compound is the first compound of claim 26. Methods of using this compound are taught from pages 17 to 18. It is noted that the abstract says the compounds of WO 2004/076453 **may** be useful for the treatment of diseases (see abstract).

The applied reference has five applicants in common with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Peters et al. (WO 2004/076453, published 10 September 2004, international filing date of 4 February 2004, has priority to 60/449871, filed 27 February 2003).

Determining the scope and contents of the prior art

Peters et al. teach compound 23 (of page 11). In this compound instant variable n is two, A' is furan, L is a bond, A" is phenylene, and B is NH(CO)phenyl. Pharmaceutical compositions are taught from pages 19 to 20. Compound 23 is prepared on page 21 (example 1). This compound is the first compound of claim 26. Methods of using this compound are taught from pages 17 to 18. It is noted that the abstract says the compounds of WO 2004/076453 **may** be useful for the treatment of diseases (see abstract).

Ascertaining the differences between the prior art and the claims at issue

In compound 2 of claim 25, the terminal phenyl group is attached to the rest of the compound at the 3-position. In example 1 of Peters et al., the point of attachment is the 4-posiiton to the terminal phenyl ring.

Resolving the level of ordinary skill in the pertinent art

Those of relative skill in the art are those with level of skill of the authors of the references cited to support the examiner's position. The relative skill of those in this art is MD's, PhD's, or those with advanced degrees and the requisite experience in preparation of compounds of the elected group.

Considering objective evidence present in the application indicating obviousness or nonobviousness

In re Norris (84 USPQ 458) teaches "Counsel for applicant in their brief acknowledge that the record herein does not establish new and useful compound defined by the rejected claim possesses one or more specifically identified properties to be recognized as unobvious or unexpected, as measured by every conceivable standard. Since the product claimed herein admittedly possesses no unexpected characteristics or properties, in view of what has hereinbefore been said, it is not patentable."

The only difference between example 1 of Peters et al. and the second compound of claim 26 is the point of attachment to the phenyl ring. It is taught that this compound could be useful in the same field of study as the instant application. Thus, example 1 of Peters et al. renders compound of claim 26 obvious.

Conclusion

14. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NOBLE JARRELL whose telephone number is (571)272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Noble Jarrell/
Examiner, Art Unit 1624

/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624